

(12) United States Patent

Nirogi et al.

(54) HETEROARYL COMPOUNDS AS 5-HT₄ RECEPTOR LIGANDS

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Field of Classification Search

See application file for complete search history.

(56)**References Cited**

U.S. PATENT DOCUMENTS

5,854,261	A	12/1998	Bosmans	514/320
7,943,645	B2	5/2011	Chan et al	514/364

US 9,636,335 B2 (10) Patent No.:

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2006/0194842 A1 8/2006 Uchida 8/2008 Noguchi 2008/0207690 A1 2008/0255113 A1 10/2008 Kato 2008/0269211 A1 10/2008 Ishibashi

FOREIGN PATENT DOCUMENTS

WO WO 93/02677 A1 2/1993 5/1997 9717345

OTHER PUBLICATIONS

Karran, E. et al. The amyloid cascade hypothesis for Alzheimer's disease: an appraisal for the development of therapeutics. Nature. 2011, vol. 10, p. 698.*

Schmitz, C. et al. Hippocampal Neuron Loss Exceeds Amyloid Plaque Load in a Transgenic Mouse Model of Alzheimer's Disease. American Journal of Pathology. 2004, vol. 164, p. 1495.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR. American Psychiatric Association. 2000, pp. 885-886.*

Bostrom, J. et al. Oxadiazoles in Medicinal Chemistry. Journal of

Medicinal Chemistry. 2012, vol. 55, p. 1817. J. Bockaert et al., "5-HT4 Receptors" Current Drug Targets— CNS & Neurological Disorders 3:39-51 (2004). S. Consolo et al., "5-HT4 receptor stimulation facilitates acetylcho-

line release in rat frontal cortex" NeuroReport 5:1230-1232 (1994). C.J. Swain et al., "Novel 5-HT3 Antagonists. Indole Oxadiazoles" J. Med. Chem. 34:140-151 (1991).

Brown, Arthur M. and Rampe, David, "Drug-Induced Long QT Syndrome: Is HERG the Root of All Evil", Pharmaceutical News,

Published 2000, pp. 15-20, vol. 7, No. 4.
Beattie, D.T., et al, "An In Vitro Investigation of the Cardiovascular Effects of the 5-HT 4 Receptor Selective Agonists, Velusetrag and TD-8954", Vascular Pharmacology (2012) pp. 1-28 doi:10.1016/j. vph.2012.11.002

Langlois, Michel & Fischmeister, Rodolphe, "5-HT4 Receptor Ligands: Applications and New Prospects", Journal of Medicinal Chemistry, Published 2003, pp. 319-44, vol. 46, No. 3.

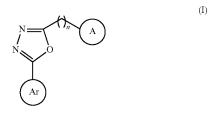
Letty, S., et al, "5-HT4 Receptors Improve Social Olfactory Memory in the Rat", Neuropharmacology, published 1997, pp. 681-687, vol. 36, No. 4/5.

(Continued)

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ABSTRACT

The present invention relates to novel compounds of formula (I), and their pharmaceutically acceptable salts and compositions containing them.



The present invention also relates to a process for the preparation of above said novel compounds, and their pharmaceutically acceptable salts. The compounds of formula (I) are useful in the treatment of various disorders that are related to 5-HT₄ receptors.

21 Claims, No Drawings